

ATTY. DOCUMENT NO.  
30727.0013.CIP1SERIAL NO.  
09/518,501LIST OF PATENTS AND OTHER ITEMS FOR APPLICANT'S  
INFORMATION DISCLOSURE STATEMENT

(Use several sheets if necessary)

APPLICANT:  
METABASIS THERAPEUTICS, INC.FILING DATE:  
March 5, 1999GROUP:  
1614

## U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB CLASS	FILING DATE
AA		3,018,302	01.23.62	Bielefeld, et al.			
AB		5,157,027	10/20 92	Biller, et al.			
AC		5,658,889	8/19/97	Gruber, et al.			

## FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB CLASS	TRANSLATION	
							YES	NO
AD		0 002 062 A	30.05.79	EP (Abstract)				
AE		0 072 531 A	23.02.83	EP (Abstract)				
AF		0 158 057 A	16.10.85	EP (Abstract)				
AG		0 180 276	28.12.88	EP				
AH		0 261 283	22.09.86	EP				
AI		0 161 955 A	21.11.85	EPO				
AJ		0 338 372 A	25.10.89	EPO				
AK		0 353 692 A	07.02.90	EPO				
AL		0 481 214 A	22.04.92	EPO				
AM		492 738 A	30.06.70	CH				
AN		16 93 219 A	17.09.70	DE (Abstract)				

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TC	AO 35 12 781 A1	10.04.85	DE (and English language U.S. Patent No. 4,952,740)				
	AP 96/01267 A	18.01.96	WO				
	AQ 97/03679 A	06.02.97	WO				
	AR 98/09668 A	12.03.98	WO				
	AS 98/39342	11.09.98	WO				
	AT 98/39343	11.09.98	WO				
	AU 98/39344	11.09.98	WO				

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, etc.)

AV	"Patent Abstracts of Japan," Vol. 1998, No. 1, 30 January 1998 & JP 09 241284 A (Yamishata Koji; Nippon Soda Co. Ltd), 16 September 1997
AW	DeLombaert, et al., "N-Phosphonomethyl Dipeptides and Their Phosphonate Prodrugs, a New Generation of Neutral Endoproteptidase (NEP, EC 3.4.24.11) Inhibitors, <u>J. Med. Chem.</u> 37: 498-511 (1994)
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BE	Hunston, et al., "Synthesis and Biological Properties of Some Cyclic Phosphotriesters Derived from 2'-Deoxy-5-fluorouridine," <u>J. Med. Chem.</u> 27: 440-444 (1984)
BF	Kryuchkov, et al., <u>Izv. Akad. Nauk SSSR, Ser. Khim.</u> 6: 1201-1248 (1987)
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BK	Neidlein, et al., "Mild Preparation of 1-Benzoyloxyiminoalkylphosphonic Dichlorides: Application to the Synthesis of Cyclic Phosphonic Diesters and Cyclic Monoester Amides," <u>Heterocycles</u> 35: 1185-1203 (1993)

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BL	Nifant'ev, et al., "1,3,2, - Diazaphosphorinanes", <u>Zh. Obshch. Khim.</u> , Vol. 49, No. 1, 1979, Pages 64-74 (and English version as translated in corresponding English language publication)
BM	Nifant'ev, et al., "Synthesis and Structure of Some Stable Phospholane-Phospholanes," <u>Phos. Sulfur &amp; Silicon</u> 113, 1-13 (1996)
BN	Predvoditelev D., et al., "Glycero-2-hydroxymethylene phosphates" <u>Journal of Organic Chemistry of the USSR (English Translation</u> 13:1489-1492 (1977))
BO	Predvoditelev, D. et al., "Synthesis of lipids and their models on the basis of glycerol alkylene phosphites. V. Cyclic phosphatidylglycerol and phosphatidylhydroxyhomocholine" <u>Journal of Organic Chemistry of the USSR (English Translation</u> 17:1156-1165 (1981)
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BT	Zon, et al., "4 Cyclophosphamide Analogues," <u>Prog. Med. Chem.</u> 19: 205-246 (1982)

*All duplicates*

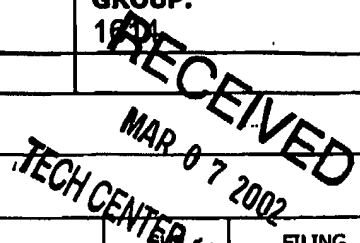
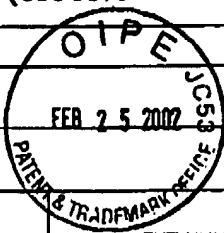
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<b>FORM PTO-1449</b>		<b>ATTY. DOCKET NO.</b> 30727.001 IP1	<b>SERIAL NO.</b> 09/518,501
<b>LIST OF PATENTS AND OTHER ITEMS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT</b>  <i>HU</i> (Use several sheets if necessary)		<b>APPLICANT:</b> METABASIS THERAPEUTICS, INC.	
		<b>FILING DATE:</b> March 5, 1999	<b>GROUP:</b> 1601

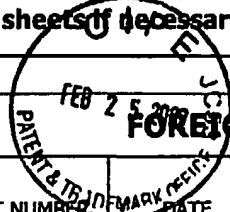


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<i>TUM</i>	AA	3,018,302	01/23/62	Bielefeld, et al.	260	461	—
<i>TUM</i>	AB	5,157,027	10/20/92	Biller, et al.	514	167	—
<i>TUM</i>	AC	5,658,889	8/19/97	Gruber, et al.	514	43	—

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<i>TUM</i>	AD	0 002 062 A1	30.05.79	EP (and English language Abstract)				
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	AL	0 481 214 B1	22.04.92	EPO				
	AM	492 738	30.06.70	CH (and English language Abstract)				
<i>✓</i>	AN	987,378	17.09.70	UK				

<b>EXAMINER:</b> <i>James M. Mc...</i>	<b>DATE CONSIDERED:</b> <i>7/8/02</i>
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<div style="text-align: center;">  <b>FOREIGN PATENT DOCUMENTS</b> </div>							
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<i>Am</i>	AO	35 12 781 A1	10.04.85	DE (and English language U.S. Patent No. 4,952,740)			
	AP	96/01267	18.01.96	WO			
	AQ	97/03679	06.02.97	WO			
	AR	98/09668	12.03.98	WO			
	AS	98/39342	11.09.98	WO			
	AT	98/39343	11.09.98	WO			
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<i>✓</i>	AZ	Farquhar, et al., "Biologically Reversible Phosphate-Protective Groups," <u>J. Pharm. Sci.</u> 72(3): 324-325 (1983)

<b>EXAMINER:</b> <i>Thomas M. Chie</i>	<b>DATE CONSIDERED:</b> <i>7/9/02</i>
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**OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, etc.)**

CM	BA	Farquhar, et al., "Synthesis and Biological Evaluation of 9-[5'-(2-Oxo-1,3,2-oxazaphosphorinan-2-yl)-β-D-arabinosyl]adenine and 9-[5'-(2-Oxo-1,3,2-dioxazaphosphorinan-2-yl)-β-D-arabinosyl]adenine: Potential Neutral Precursors of 9-[β-D-Arabinofuranosyl]adenine 5'-Monophosphate," <u>J. Med. Chem.</u> 28: 1358-1361 (1985)
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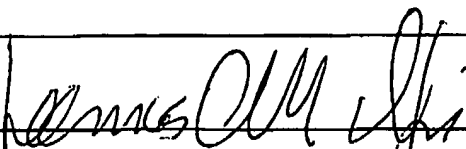
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March 10/31/2002. OMB 0851-0031

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Substitute for form 1449A/PTO

Complete If Known

# INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 1 of 2

Application Number 09/518,501  
Filing Date March 3, 2000  
First Named Inventor Erlon  
Group Art Unit 1624  
Examiner Name T. McKenzie  
Attorney Docket Number 030727.0013.CIP1

## U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No. <sup>1</sup>	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code <sup>2</sup> (if known)			

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		Office <sup>4</sup>	Number <sup>4</sup>	Kind Code <sup>2</sup> (if known)				

## NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
	AA	Coppi, et al., "Lewis Acid Mediated Condensation of Alkenols and Aldehydes. A Selective Synthesis of Tetrahydropyrans and Oxepanes," J. Org. Chem., Vol. 53, No. 4, 911-913 (1988)	
	AB	Lohr et al., "Targeted chemotherapy by intratumor injection of encapsulated cells engineered to produce CYP2B1, and ifosfamide activating cytochrome P450," Gene Therapy, 5, 1070-1078 (1988).	
	AC	Bijsterbosch, et al., "Disposition of the Acyclic Nucleoside Phosphonate (S)-9-(3-Hydroxy-2-Phosphonylmethoxypropyl)Adenine," Antimicrobial Agents and Chemotherapy, Vol. 42, p. 1146-1150 (May 1998).	
	AD	de Waziers, et al., "Cytochrome P 450 Isoenzymes, Epoxide Hydrolase and Glutathione Transferases in Rat and Human Hepatic and Extrahepatic Tissues1," The Journal of Pharmacology and Experimental Therapeutics, Vol. 253, No.1, p. 387-394 (1989).	

Examiner Signature

Date Considered

2/12/03

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<sup>1</sup> Unique citation designation number. <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

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**(use as many sheets as necessary)**

**Complete If Known**

Application Number	09/518,501
Filing Date	March 5, 1999
First Named Inventor	Erion
Group Art Unit	1624
Examiner Name	T. McKenzie
Attorney Docket Number	030727.0013.CIP1

Sheet	2	of	2
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## NON PATENT LITERATURE DOCUMENTS

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Substitute for form 1449A/PTO		Complete if Known			
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)		Application Number	09/518,501		
		Filing Date	March 3, 2000		
		First Named Inventor	Erion et al.		
		Group Art Unit	1824		
		Examiner Name	McKenzie, T.		
Sheet	1	of	1	Attorney Docket Number	45198.00013.RCE (CIP1)

U.S. PATENT DOCUMENTS						
Examiner Initials <sup>1</sup>	Cite No. <sup>1</sup>	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code <sup>2</sup> (if known)			
[initials]		6,054,587		Reddy et al.	04/25/00	
		6,110,903		Kasibhatla et al.	08/29/00	
		6,284,748		Dang et al.	09/04/01	
		6,294,672		Reddy et al.	09/25/01	
		6,312,662		Erion et al.	11/06/01	
		6,399,782		Kasibhatla et al.	06/04/02	
		6,489,476		Dang et al.	12/03/02	

FOREIGN PATENT DOCUMENTS							
Examiner Initials <sup>1</sup>	Cite No. <sup>1</sup>	Foreign Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>3</sup>
		Office <sup>1</sup>	Number <sup>1</sup>				

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Examiner Initials <sup>1</sup>	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.			T <sup>2</sup>

Examiner Signature	<i>Tom McKen</i>	Date Considered	4/16/04
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## INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet	1	of	1
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**Complete if Kn wn**

<b>Application Number</b>	09/518,501
<b>Filing Date</b>	March 3, 2000
<b>First Named Inventor</b>	Erion et al.
<b>Group Art Unit</b>	1624
<b>Examiner Name</b>	T. McKenzie
<b>Attorney Docket Number</b>	45198.00013.RCE



## U.S. PATENT DOCUMENTS

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## FOREIGN PATENT DOCUMENTS

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## NON PATENT LITERATURE DOCUMENTS

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		FARQUHAR et al., "Synthesis and Antitumor Evaluation of Bis[pivaloyloxy)methyl] 2'-Deoxy-5-fluorouridine 5'-Monophosphate (FdUMP): A Strategy to Introduce Nucleotides into Cells," <u>J. Med. Chem.</u> , 37:3902-3909 (1994).	
		LEFEBVRE, et al., Mononucleotide Phosphotriester Derivatives with S-Acyl-2-thioethyl Bioreversible Phosphate-Protecting Groups: Intracellular Delivery of 3'-Azido-2',3'-dideoxythymidine 5'-Monophosphate," <u>J. Med. Chem.</u> , 38:3941-3950 (1995).	

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Sheet 1 of 3

## Complete if Known

Application Number 09/518,501  
Filing Date March 3, 2000  
First Named Inventor Erion et al.  
Group Art Unit 1624  
Examiner Name T. McKenzie  
Attorney Docket Number 032465.00013.RCE (CIP1)

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## FOREIGN PATENT DOCUMENTS

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		Office <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>3</sup> (if known)				

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g		Beaucage and Iyer, "The Synthesis of Modified Oligonucleotides by the Phosphoramidite Approach and Their Applications," <u>Tetrahedron</u> , 49(28):6123-6194 (1993).	
		Borch and Millard, "The Mechanism of Activation of 4-Hydroxycyclophosphamide," <u>J. Med. Chem.</u> , 30:427-431 (1987).	
		Cooper et al., "Use of Carbohydrate Derivatives for Studies of Phosphorus Stereo-chemistry. Part II. Synthesis and Configurational Assignments of 1,3,2-Oxathiaphosphorinan-2-ones and 1,3,2-Dioxaphosphorinan-2-thiones," <u>J. Chem. Soc., Perk. Trans. 1</u> , (10):1049-1052 (1974).	
		De Clercq et al., "A Novel Selective Broad-spectrum Anti-DNA Virus Agent," <u>Nature</u> , 323:464-467 (1986).	
		Farquhar et al., "Synthesis and Antitumor Evaluation of Bis[(pivaloyloxy)methyl] 2'-Deoxy-5-fluorouridine 5'-Monophosphate (FdUMP): A Strategy to Introduce Nucleotides into Cells," <u>J. Med. Chem.</u> , 37:3902-3909 (1994).	

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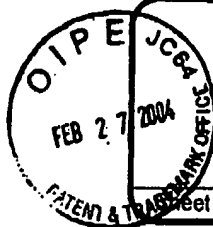
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## Complete if Known

Application Number	09/518,501
Filing Date	March 3, 2000
First Named Inventor	Erlon et al.
Group Art Unit	1624
Examiner Name	T. McKenzie
Attorney Docket Number	032465.00013.RCE (CIP1)

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J		Friis and Bundgaard, "Prodrugs of Phosphates and Phosphonates: Novel Lipophilic $\alpha$ -acyloxyalkyl Ester Derivatives of Phosphate- or Phosphonate Containing Drugs Masking the Negative Charges of these Groups," <u>Euro. J. Pharm. Sci.</u> , 4:49-59 (1996).	
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		Khorana et al., "Cyclic Phosphates. III. Some General Observations on the Formation and Properties of Five-, Six- and Seven-membered Cyclic Phosphate Esters," <u>JACS</u> , 79:430-436 (1957).	
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		Ramachandran et al., "Efficient General Synthesis of 1,2- and 1,3-diols in High Enantiomeric Excess via the Intramolecular Asymmetric Reduction of the Corresponding Ketoalkyl Diisopinocampheylborinate Intermediates," <u>Tetrahedron</u> , 38(5):761-764 (1997).	

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Filing Date	March 3, 2000
First Named Inventor	Erion et al.
Group Art Unit	1624
Examiner Name	T. McKenzie
Attorney Docket Number	032465.00013.RCE (CIP1)

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g		Starrett, Jr. et al., "Synthesis, Oral Bioavailability Determination, and <i>in Vitro</i> Evaluation of Prodrugs of the Antiviral Agent 9-[2-(Phosphonomethoxy)ethyl]adenine (PMEA)," <u>J. Med. Chem.</u> , 37:1857-1864 (1994).	
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		Zon et al., "NMR Spectroscopic Studies of Intermediary Metabolites of Cyclophosphamide. A Comprehensive Kinetic Analysis of the Interconversion of <i>cis</i> - and <i>trans</i> -4-Hydroxycyclophosphamide with Aldophosphamide and Concomitant Partitioning of Aldophosphamide Between Irreversible Fragmentation and Reversible Conjugation Pathways," <u>J. Med. Chem.</u> 27:466-485 (1984).	

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4/16/07

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